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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/771,696	02/04/2004	Kazunari Nakao	PC 9985B	3929

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EXAMINER	
STOCKTON, LAURA	

ART UNIT	PAPER NUMBER
1626	

DATE MAILED: 07/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/771,696	NAKAO ET AL.	
	Examiner	Art Unit	
	Laura L. Stockton, Ph.D.	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 April 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

JC

DETAILED ACTION

Claims 26-39 are pending in the application.

Election/Restrictions

Applicants' election with traverse of Group I, and the species found in instant claim 24, in the reply filed on October 13, 2004 was acknowledged in the previous Office Action. The requirement was deemed proper and made FINAL in the previous Office Action.

Subject matter not embraced by elected Group I is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention. Applicant timely traversed the restriction (election) requirement in the reply filed on October 13, 2004.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 26-39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

No support in the specification or originally filed claims can be found for the phrase "A method for the treatment of a disorder or condition mediated by an EP4 receptor" and every disorder or condition listed (see instant claim 26) associated with the EP4 receptor

found in newly added independent claim 28. Previously, independent claim 13 (now cancelled) claimed:

13. (Previously presented) A method for the treatment of a disorder or condition mediated by prostaglandin, in a mammalian subject including a human, comprising administering to

Applicants did not state where {page number(s) and line number(s)} support could be found for the above noted phase language. Applicants should specifically point out the support for any amendments. See M.P.E.P. §§ 714.02 and 2163.06. Therefore, the claims lack written description as such.

Claims 26-39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which

it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The nature of the invention

Applicants are claiming a method for the treatment of all disorders or conditions mediated by an EP4

receptor. From the reading of the specification, it appears that Applicants are asserting that the embraced compounds, because of their mode action, would be useful for treating numerous disorders or conditions such as AIDS, Alzheimer's disease, all immune diseases, all autoimmune diseases, all gastrointestinal cancers, all inflammation associated disorders (i.e., cancer), cellular neoplastic transformations or metastic tumor growth, etc.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that cancer therapy, for example, remains highly unpredictable. The various types of cancers have different causative agents, involve different cellular mechanisms, and consequently, differ in treatment protocol. It is known (see Golub et al., Science, Vol. 286, October 15, 1999, pages 531-537) that the challenge of cancer

treatment has been to target specific therapies to pathogenetically distinct tumor types, to maximize efficacy and minimize toxicity. Cancer classification has been based primarily on morphological appearance of the tumor and that tumors with similar histopathological appearance can follow significantly different clinical courses and show different responses to therapy (Golub et al., Science, Vol. 286, October 15, 1999, pages 531-537). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face. Additionally, for example, inflammation is a process that can take place in virtually any part of the body. There is a vast range of forms that it can take, causes for the problem, and biochemical pathways.

The amount of direction or guidance present and the presence or absence of working examples

The only direction or guidance present in the instant specification is found on pages 101-104 for testing the compounds. That a single class of compounds can be used to treat all the disorders or conditions embraced by the claims is an incredible finding for which Applicants have not provided supporting evidence. Applicants has not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use for treating all conditions by administering the instant claimed compounds.

The breadth of the claims

The breadth of the claims is the treatment of all disorders or conditions mediated by an EP4 receptor.

The quantity of experimentation needed

The nature of the pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities for which susceptible neoplasm. The quantity of experimentation needed would be undue when faced with the lack of direction and guidance present in the instant specification in regards to testing of all of the various disorders or conditions in instant independent claim 28 and when faced with the unpredictability of, for example, the cancer therapy art. Thus, factors such as "sufficient working examples", "the level of skill in the art" and predictability, etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims.

The level of the skill in the art

Even though the level of skill in the cancer therapy art, for example, is very high, based on the

unpredictable nature of the invention and state of the prior art and lack of guidance and direction for all of the various disorders or conditions embraced by instant independent claim 28 (or more specific in instant claim 26), one skilled in the art could not use the claimed invention without undue experimentation.

Response to Arguments

Applicants' arguments filed April 29, 2005 have been fully considered. Applicants argue that the instant specification enables any person skilled in the art to which the invention pertains to use the instant invention commensurate in scope with amended claim 26. In response, claim 26 is not an independent claim. Claim 26 depends from the much broader newly added independent claim 28.

Applicants argue that: (1) one skilled in the art would find the asserted utility of the claimed

compounds consistent with knowledge in the art at the time of the filing of the present invention; and (2) the scientific literature establishes a direct relationship between prostaglandin EP4 receptor antagonists and the claimed utilities.

All of Applicants' arguments have been considered but have not been found persuasive. As stated above, the nature of the pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. That a single class of compounds can be used to treat all the disorders or conditions embraced by the claims is an incredible finding. The literature references submitted by Applicants have all been reviewed. Even in some of Applicants' submissions it is acknowledged that the nexus between the EP4 receptor and the treatment of, for example, metabolic bone diseases, is still in an exploratory stage (see page 19822, column 2, last paragraph in Miyaura et al., The

Journal of Biological Chemistry, Vol. 275, No. 26, June 30, 2000, pages 19819-19823). Therefore, the lack of enablement rejection is proper.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 26-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 28, under the definition of the Y variable, the phrase "one of _Y^1" should be changed to "one of Y^1". In claims 28 and 29, under the definition of the Z variable, it is not possible to have a C_1 alkenyl or alkynyl group. In claim 28, under the definition of the Q^2 variable, "halo-substituted $C1_{1-4}$ alkoxy" should be changed to "halo-substituted C_{1-4}

alkoxy". In claims 33-36, under the definition of the L variable, "trifluoromethyloxy" is misspelled. In claim 26, an "and" should be added before kidney disease and the semi-colon should be deleted after kidney disease.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 26-39 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of copending Application No. 09/977,761 and claims 1-6 of 10/411,491. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claimed method of using the products of the instant formula is generically embraced by the methods found in 09/977,761. See, specifically, instant claims 27 and 28; claims 1 and 5 in 09/977,761; and claims 4 and 5 in 10/411,491.

The indiscriminate selection of "some" among "many" is *prima facie* obvious, *In re Lemin*, 141 USPQ 814 (1964). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity (e.g., treating rheumatoid arthritis).

One skilled in the art would thus be motivated to administer products embraced by 09/977,761 and

10/411,491 for the methods claimed in 09/977,761 and 10/411,491 to arrive at the instant claimed invention with the expectation of treating disorders or conditions such as pain and rheumatoid arthritis. The instant claimed invention would have been suggested and therefore, obvious to one skilled in the art. A strong case of *prima facie* obviousness has been established.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

On page 22 in Applicants' Remarks section filed April 29, 2005, Applicants state that a Terminal Disclaimer will be timely filed when all other issues have been resolved.

Conclusion

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura L. Stockton whose telephone number is (571) 272-0710. The examiner can normally be reached on Monday-Friday from 6:15 am to 2:45 pm. If the examiner is out of the Office, the examiner's supervisor, Joseph McKane, can be reached on (571) 272-0699.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

The Official fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Laura L. Stockton, Ph.D.
Patent Examiner
Art Unit 1626, Group 1620
Technology Center 1600

July 22, 2005